

THE ANTECEDENTS OF BLOOD TRANSFER *

LESTER BLUM and WILLIAM M. NELSON, Ph.D.

THE association of blood with life itself is among the primitive concepts of man. In the picturesque phraseology of the Old Testament, blood is a synonym for vitality, emotion and heritage. It constitutes the basis of one of the plagues described in Exodus when Moses caused all the rivers and streams of Egypt to run red.¹ It is not surprising that both Pliny and Celsus describe the patricians rushing from their seats in the Coliseum down into the arena to drink the freshly flowing blood of dying gladiators.²

The thought that all these vital properties could be transmitted by the act of transfusion is of ancient origin. A rational approach to this end, however, necessarily awaited a clear understanding of the nature of the circulation. This was provided by William Harvey in his *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus*, published at Frankfort in 1628.

Although animal and human blood had already been administered by infusion, the first successful transfusions in animals were evidently performed on dogs by Richard Lower at Oxford in 1665.³ He connected the blood vessels with quills and silver tubes.

Just two years later, on June 15, 1667, the first recorded transfusion in man was accomplished by Jean Baptiste Denis at Paris. In a famous letter⁴ written ten days thereafter, Denis stated that in his preliminary experimental work none of nineteen dogs died. He connected the crural artery of the donor animal to the jugular vein of the recipient. He was thus emboldened to transmit 9 ounces of blood from the carotid artery of a lamb to a sixteen-year old asthenic youth who had been repeatedly bled for fever.

Denis' second case was that of a forty-five year old man who was first bled 10 ounces and then given 20 ounces from the crural artery

* Presented before the Section on Historical and Cultural Medicine of The New York Academy of Medicine, January 12, 1955. Manuscript received March 1955.
From the Beekman-Downtown Hospital, New York.

of a lamb. Immediately following the procedure, the patient killed and dressed the lamb and then went off to a tavern to drink part of the money "given him for the day's business". The conclusion is inescapable that this account establishes the priority of the first paid recipient long before paid donors appeared on the scene.

As a result of difficulties encountered in transfusing a third patient, Denis suffered for years because of litigation with an ungrateful widow. The procedure fell into disrepute and little was done in this field for another century and a half.

In 1821, Prevost and Dumas showed that exsanguinated animals could be revived by transfusion but not by serum or water solution.

Several years later, in 1828, James Blundell⁵ reported his rediscovery of transfusion in the treatment of postpartum hemorrhage. In a classic article in the *Lancet* he described eleven transfusions performed despite failure in the first four attempts. Blundell used human donors and emphasized that the blood of an alien species was unsuitable. He warned about the necessity for careful observation of the recipient throughout the procedure. There is an illustration of his "Gravitator" which was a metal channel with an upper basin for collection of the standing donor's blood leading down to a silver tube placed in the basilic vein of the recumbent recipient. The passage was flushed with clean water or warm milk at intervals to wash out clots.

It should be noted that at this time there lived and worked the great Jean Leonard Marie Poiseuille (1799-1869) who is considered the father of rheology by the physicists who recognized his genius many years before his fellow physicians appreciated his contributions. The importance of Poiseuille's work in basic concepts of blood flow and circulatory dynamics is only being understood in our time.

A generation after Blundell, Franz Gesellius⁶ developed an ingenious apparatus for the collection of capillary blood for transfusion. It is of purely historical interest.

Although Landois,⁷ in 1874, demonstrated that the serum of one species agglutinated or dissolved the corpuscles of others, it is surprising to note that at the German Surgical Congress of that year, thirty-one transfusions with sheep's blood were reported.

In the last quarter of the Nineteenth Century, despite the great interest in this procedure and the arguments as to whether blood should be injected towards the heart or away from it, the large number of



Fig. 1—The Ancient Syringe Ritual of the Hindu. (From Ewbank, T.¹⁷ *Hydraulic and other machines*. New York, Scribner, 1870. Reprinted by permission of the publisher.)

adverse reactions resulted in far more saline solution being used than blood. It was not until the dawn of the Twentieth Century that the most important step in the establishment of transfusion as a scientific procedure of the highest therapeutic importance was made. In 1901 Landsteiner⁸ described the blood types and laid the foundation for this entire branch of hematology. His work explained the troublesome and unpredictable reactions of the past and laid the basis for the removal of most of the risk of transfusion. Several years were to pass before the practical application of his contribution by Ottenberg⁹ became part of clinical technique.

Although direct transfusion by syringe was systematized by Lindeman¹⁰ and Unger¹¹ by the time of the outbreak of World War I, the procedure did not always run off smoothly and required operating room conditions to insure successful handling. The chief problem remaining was that of controlling the physical state of blood so that it stayed fluid and lost little of its other properties.

In all probability, the first step in this direction was taken by Poiseuille,¹² in 1823 when he employed potassium bicarbonate solution to keep the tubing clear in his studies of blood pressure by direct manometry in millimeters of mercury. In the latter Nineteenth Century sodium phosphate and mechanical defibrination were used to retard clotting. In the same year as Landsteiner's publication, Bordet and Gengou¹³ showed that clotting could be inhibited by physical means such as the paraffin coating of vessels and tubing. A significant step forward in the efficient handling of blood was the observation of Hustin¹⁴ that sodium citrate and dextrose indefinitely retarded clotting and permitted the precise, unhurried, clean handling of blood which led to the indirect method of transfusion most common today. The first citrated transfusion, credited to Luis Agote,¹⁵ was performed in Buenos Aires on November 14, 1914. At the same time Lewisohn¹⁶ was solving the problem in New York.

Although heparin, the ideal and natural anticoagulant, was not to be generally available for another twenty-five years, it is a sad fact that all the requisites for the use of blood, as we know them today, were at hand shortly after World War I got under way. Blood banks were not established until thirty years later. In short, the real obstacle to progress was the remarkable lack of imagination shown by our profession in being unable to benefit immediately from the advances discovered in the laboratory.

This, then, is a bare outline of the major steps necessary to provide the large amounts of blood used in surgery today. The successful storage for days outside the body of this tissue in the fluid state, not only provided the ideal remedy for hemorrhage, shock and debilitating disease but also made possible the exploitation of other vital functions of blood such as those connected with oxygenation and the excretion of waste products.

THE CONDUCTION OF BLOOD OUTSIDE VASCULAR CHANNELS

In Lower's original experiments the blood vessels were connected with quills and silver tubes. Blundell,⁵ recognizing the importance of pressure in the introduction of satisfactory quantities before clotting took place, employed his "Gravitator" which was a rather complex, elongated silver tube for establishing a head of pressure equal to most of the height of the standing donor. This simple apparatus takes prece-



Fig. 2—The Roman Piston Bellows. (From Ewbank, T.¹⁷
Hydraulic and other machines. New York, Scribner, 1870.
Reprinted by permission of the publisher.)

dence over the syringe in the actual transfer of blood. In the latter Nineteenth Century syringes with stopcocks were employed.

The syringe is mentioned as an instrument in the embalming procedure of ancient Egypt. It was employed by the Hindus in religious rites that date back to antiquity.¹⁷ It reached its highest development in transfusion in the apparatus of Unger.¹¹ Its use for the transfer of large amounts of blood over long periods of time is rather limited because the turbulence which is a necessary part of its rapid function results in a forbidding degree of hemolysis. In the latter Nineteenth Century there also appeared the milking type of pump for transfusion. This was latterly preferred by von Issekutz¹⁸ and independently by DeBakey.¹⁹ Movement of the blood column was obtained by alternate compression and relaxation of the tube through which the blood ran. This could be effected by rollers or by separate levers. It is considered satisfactory enough today to be the most common type of propellant used in extracorporeal shunting.

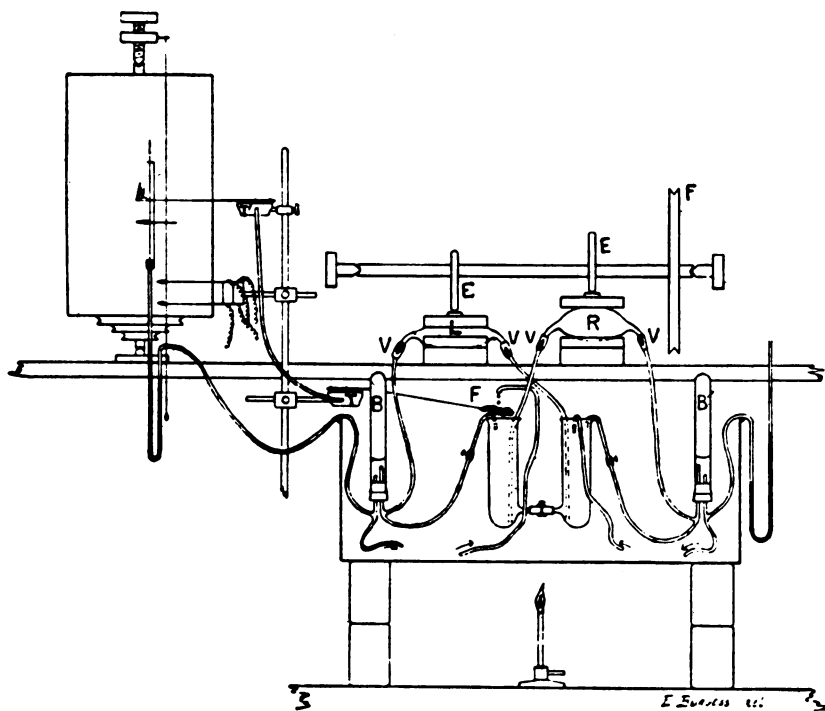


Fig. 3—The Blood Pump of Embley and Martin—1905. (From Embley, E. H. and Martin, C. J.²⁰ in *Journal of Physiology* 32:147-58, 1905. Reprinted by permission of the publisher, Cambridge University Press.)

Other types of rotary or reciprocating pumps have been used clinically and in the laboratory during the last fifty years. Some are direct modifications of pump types used in antiquity for irrigation such as the Chinese noria, the Persian sakias, the Roman piston bellows and the Egyptian tympanum. All of these are either rotary or reciprocating types.

The problem of propelling blood outside the body arose in the laboratory in the latter Nineteenth and early Twentieth Centuries when studies of the physiology of organs and tissues under partially controlled conditions became feasible. Although too much attention did not have to be paid to the avoidance of blood cell destruction there was an obvious advantage in minimizing this and other untoward effects.

In 1905, Embley and Martin²⁰ devised an ingenious double circulation system that propelled the blood through the lung for oxygenation

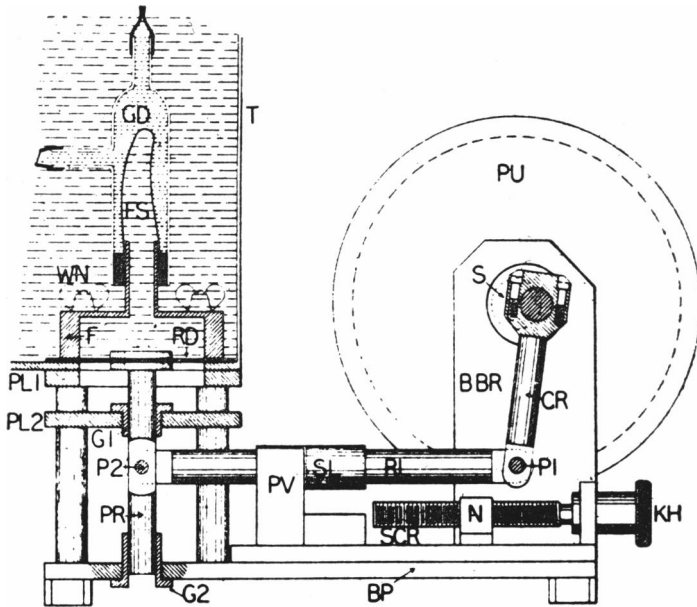


Fig. 4—The Dual Blood Pump of Dale and Schuster—1927. (From Dale, H. H. and Schuster, E. H. J.²¹ in *Journal of Physiology* 64:356-84, 1927. Reprinted by permission of the publisher, Cambridge University Press.)

and then into the arterial tree for clearance through the kidney. They used a reciprocating type pump with rubber bladders compressed by the platforms. Variations of this system were employed thereafter until 1927 when Dale and Schuster²¹ described their double perfusion pump in which an attempt was made to maintain sterility and avoid as much cell destruction as possible.

Mechanical improvements in the propulsion of blood have progressed with increasing knowledge of hemodynamics. The recent development of blood pumps is an attempt to meet the challenge of shunting blood outside the body for oxygenation or urea clearance with as little change in its physical characteristics as possible. The study of coagulation, changes in pH, osmotic pressure, viscosity, elasticity, turbulence and foaming is all part of this endeavor.

THE ARTIFICIAL KIDNEY

Ever since Ludwig's exposition of the nature of the function of the mammalian kidney, the idea of a mechanical substitute seemed a

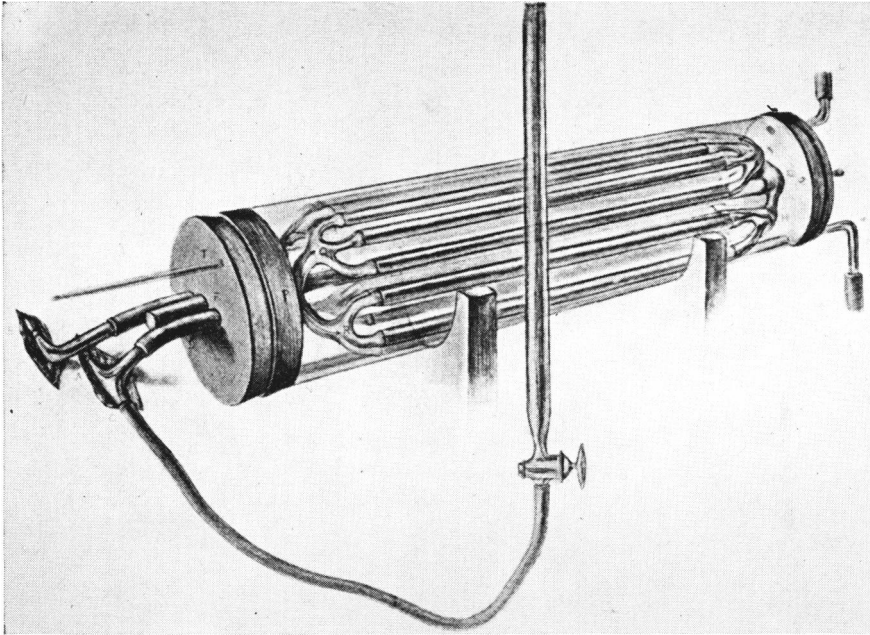


Fig. 5—Perspective View of Vividiffusion Apparatus; Earlier Form with Sixteen Tubes. The Artificial Kidney of Abel, Rowntree and Turner—1913. (From Abel, J. J., Rowntree, L. G. and Turner, E. B.²² in *Journal of Pharmacology and Experimental Therapeutics* 5:276-316, 1913-14. Reprinted by permission of the publisher, Williams & Wilkins Co.)

feasible one. In 1913, Abel, Rowntree and Turner²² described an apparatus which was capable of removing excessive amounts of salicylates from the circulating blood. They used an instrument through which an extracorporeal circulation was maintained with glass canulas leading from an artery to a collodion tube spiral immersed in electrolyte solution and then back again to the animal. As anticoagulant, they used hirudin obtained from the ground heads of leeches. With this apparatus toxic levels of salicylate could be reduced by diffusion to within normal limits.

The concept was well presented. "In the hope of providing a substitute in such emergencies which might tide over a dangerous crisis, as well as for the important information which it might be expected to provide concerning the circumstances normally present in the blood, and also for the light that might thus be thrown on intermediary stages of metabolism, a method has been devised by which

the blood of a living animal may be submitted to dialysis outside the body and again return to the natural circulation without exposure to air, infection by microorganisms or any alteration which would necessarily be prejudicial to life."

A decade later the use of cross transfusion for the purpose of urea clearance was studied experimentally.²³ Because of the many technical problems this line of investigation was not followed for another twenty years.

In the midst of World War II, during the invasion of his homeland, Kolff²⁴ pursued the problem clinically. To him belongs the credit of making the artificial kidney a practical instrument. He used cellophane tubes with heparin as the anticoagulant.

The remarkable perfection of this apparatus by the team at the Peter Bent Brigham Hospital in this country is an outstanding accomplishment in recent years.²⁵

USE OF THE EXTRACORPOREAL SHUNT TO EXCLUDE THE HEART

The idea of having the circulation of one animal supplying an organ of another under experimental conditions was a recognized procedure by the first decade of this century.²⁶ The application of this principle to take over the burden of the entire circulation of a companion animal is, however, an endeavor of the last decade. The necessity for rendering the heart bloodless in order to place its chambers within the realm of precise, unhurried surgery is obvious. For the use of a companion in this cross transfusion or parabiotic technique it is necessary to have a controlled, dual action pump which can exchange equal amounts of arterial and venous blood over some period of time without destroying the erythrocytes or defibrinating the plasma. The companion animal serves as the oxygenator in this technique.

This particular method has been the subject of intensive investigation by Blum and Megibow,²⁷ Lillehei and Warden,²⁸ Andreasen and Watson.²⁹ In the last year Lillehei has successfully applied this method for the definitive surgical cure of interventricular septal defects and the tetralogy of Fallot.

The other type of extracorporeal shunt to permit exclusion of the mammalian heart is dependent upon the employment of an oxygenator. In this method the blood is siphoned off from the venae cavae which have been clamped off and pumped into some type of apparatus which

films the blood while exposing it to pure oxygen. It is then collected and pumped back into the arterial tree. The early oxygenators depended upon the bubbling of oxygen through blood. This method was described as early as 1882.³⁰ Later investigators recognized the resultant foaming to be due to erythrocyte destruction which resulted in the ultimate death of the animal. It was soon evident that the answer to the problem lay in the filming of the moving blood over a large surface during its exposure to oxygen. Numerous ingenious devices have been employed. These include the silk mesh curtain of Richards and Drinker,³¹ the revolving spiral sheet of Cruickshank,³² the rotating glass cylinder of Frey and Gruber³³ and the multiple disks of Hooker.³⁴

It was, however, Gibbon,³⁵ who after fifteen years of application devised his present apparatus which is remarkable for the efficiency of oxygenation and the avoidance of blood destruction. The intricate device that has been developed after years of ingenious travail has, however, not yet been consistently successful in its application to clinical problems. It appears that the chief defect is that of restoring the normal coagulating properties of the blood following the procedure. The propulsion of the blood stream in this particular apparatus is achieved by use of the peristaltic type of blood pump.

The applications of the extracorporeal shunting of blood are limitless. It is conceivable that this technique may ultimately lead to the replacement of viscera by prostheses designed to substitute for them. We are now merely on the threshold of exciting possibilities which the close collaboration of the physiologist, the physicist and the surgeon can transform into solid accomplishment.

REFERENCES

1. Exodus VII.
2. Zimmerman, L. M. Evolution of blood transfusion, *Bull. Soc. med. Hist. Chicago* 5, no. 4:44-54, 1943.
3. Success of the experiment of transfusing the blood of one animal into another, *Phil. Trans. roy. Soc. London* 1:352, 1666.
4. Letter concerning a new way of curing sundry diseases by transfusion of blood, written to M. deMontmer by J. Denis, *Phil. Trans. roy. Soc. London* 1:490, 1667.
5. Blundell, J. Observations on transfusion of blood, *Lancet* 2:321-24, 1828-1829.
6. Gesellius, F. *Capillar-Blut undefibrirtes zur transfusion*. St. Petersburg, A. Muenz, 1868.
7. Landois, L. Auflösung der rothen Blutzellen, *Zbl. med. Wiss.* 12:419-22, 1874.
8. Landsteiner, K. Ueber Agglutinationserscheinungen normalen menschlichen Blutes, *Wien. klin. Wschr.* 14:1132-34, 1901.
9. Ottenberg, R. Studies in isoagglutination; transfusion and the question of

- intravascular agglutination, *J. exp. Med.* 13:425-38, 1911.
10. Lindeman, E. Simple syringe transfusion with special cannulas, *Amer. J. Dis. Child.* 6:28-32, 1913.
 11. Unger, L. J. A new method of syringe transfusion, *J. Amer. med. Assoc.* 64: 582-84, 1915.
 12. Poiseuille, J. L. M. Recherches sur la force du cœur aortique, *Paris Thesis*, 1828, p. 166.
 13. Bordet, J. and Gengou, O. Recherches sur la coagulation du sang et les sérums anticoagulants, *Ann. Inst. Pasteur* 15:129-44, 1901.
 14. Hustin, A. Principe d'une nouvelle méthode de transfusion muqueuse, *J. Med. Baux.* 12:436-39, 1914.
 15. Agote, L. Hidrocefalia sifolitica, su tratamiento porel, neosalvarsan por via intracraneana, *An. Inst. mod. de clin. Med. Buenos Aires* 1:48-57, 1915.
 16. Lewisohn, R. A new and greatly simplified method of blood transfusion, *Med. Rec.* 87:141, 1915.
 17. Ewbank, T. *Hydraulic and other machines*. New York, Scribner, 1870.
 18. von Issekutz, B. Beiträge zur Wirkung des Insulins, *Biochem. Z.* 183:283-97, 1927.
 19. DeBakey, M. E. Simple continuous-flow blood transfusion instrument, *New Orleans med. surg. J.* 87:386-89, 1934.
 20. Embley, E. H. and Martin, C. J. Action of anaesthetic quantities of chloroform upon the blood vessels of the bowel and kidney; with an account of an artificial circulation apparatus, *J. Physiol.* 32:147-58, 1905.
 21. Dale, H. H. and Schuster, E. H. J. Double perfusion-pump, *J. Physiol.* 64: 356-84, 1927.
 22. Abel, J. J., Rowntree, L. G. and Turner, B. B. On removal of diffusable substances from circulating blood by means of dialysis, *Trans. Assoc. Amer. Phycns.* 28:51-54, 1913; also in *J. Pharmacol. exp. Therap.* 5:275-316, 1913-1914.
 23. Nyiri, W. Experimentelle Untersuchungen über gekreuzte Bluttransfusion bei Urämie, *Arch. exp. Path. Pharmacol.* 116:117-24, 1926.
 24. Kolff, W. J. Die kunstmatige nier. Kampen, Holland, J. H. Kok, 1946.
 25. Merrill, J. P. The artificial kidney, *New Engl. J. Med.* 246:17-27, 1952.
 26. Fredericq, L. Sur la circulation céphalique croissée ou échange de sang carotidien entre deux animaux, *Arch. Biol.* 10:127-30, 1890.
 27. Blum, L. and Megibow, S. J. Exclusion of the dog heart by parabiosis, *J. Mt. Sinai Hosp.* 17:38-43, 1950.
 28. Warden, H. E., Cohen, M., Read, R. C. and Lillehei, C. W. Controlled cross circulation for open intracardiac surgery, *J. Thorac. Surg.* 28:331-41, 1954.
 29. Andreasen, A. T. and Watson, F. Report on experiments concerning a donor circulation, *Brit. J. Surg.* 41:195-206, 1953.
 30. von Schroeder, W. Ueber die Bildungsstätte des Harnstoffs, *Arch. exp. Path. Pharmacol.* 15:364-402, 1882.
 31. Richards, A. N. and Drinker, C. K. An apparatus for the perfusion of isolated organs, *J. Pharmacol. exp. Therap.* 7: 467-83, 1915.
 32. Cruickshank, E. W. H. A magnetic blood oxygenator, *J. Physiol.* 82:26-32, 1934.
 33. von Frey, M. and Gruber, M. Ein Respirationsapparat für isolirte Organe, *Arch. Anat. Physiol.* 9:519-22, 1885.
 34. Hooker, D. R. The perfusion of the mammalian medulla; the effect of calcium and potassium on the respiratory and cardiac centers, *Amer. J. Physiol.* 35:200-08, 1915.
 35. Gibbon, J. H., Jr. Present status of mechanical heart and lungs, *Med. Rec. Ann.* 46:872-76, 1952.